Additionally, claims 6-23 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No 09/632,718; claims 1-20 and 53-61 of copending Application No. 09/390,719; claims 23-111 of copending Application No. 08/938,898; and claims 27-68 of copending Application No. 09/304,694.

With regard to U.S. Patent Nos. 5,475,577 and 5,672,360, it is respectfully submitted that the claims of these patents fail, at the very least, to recite or suggest the following limitations of independent claim 6 of the present application:

> *(i)...wherein the dissolution rate in-vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C is from about 12.5% to about 42.5% (by wt) opioid released after 1 hour, from about 25% to about 65% (by wt) opioid released after 2 hours, from about 45% to about 85% (by wt) opioid released after 4 hours and greater than 60% (by wt) opioid released after 8 hours,...*
>
> *(ii)...the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,...*

On this basis, Applicants respectfully request that the Examiner's double patenting rejection based upon U.S. Patent Nos. 5,475,577 and 5,672,360 be withdrawn.

With regard to U.S. Patent Nos. 6,143,322, it is respectfully submitted that this patent issued from the parent application of the present application. The claims of the present application were submitted during the prosecution of U.S. Patent No. 6,143,322, and were the subject of a restriction requirement and not prosecuted in the parent application. Under 35 U.S.C. §121, *"[a] patent issuing on an application with respect to which a requirement for restriction under this section has been made, or on an application filed as a result of such a*

requirement shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application . . ., if the divisional application is filed before the issuance of the patent on the other application." Accordingly, it is respectfully submitted that this obviousness-type double patenting rejection is improper and should be removed.

With respect to the double patenting rejections over claims 1-19 of Application No 09/632,718; claims 1-20 and 53-61 of copending Application No. 09/390,719; claims 23-111 of copending Application No. 08/938,898; and claims 27-68 of copending Application No. 09/304,694, it is noted that these rejections are provisional, and as such, terminal disclaimers will be considered upon notification that the claims are otherwise allowable.

II. Rejections under 35 U.S.C. §102

U.S. Patent No. 5,968,551 (Oshlack et al.)

Claims 6-16, 18 and 21-23 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 5,968,551 (Oshlack et al.).

This rejection is respectfully traversed. U.S. Patent No. 5,968,551 is a continuation of U.S. application Ser. No. 08/133,503 filed Oct. 7, 1993, abandoned, which is a continuation-in-part of both U.S. patent application Ser. No. 08/081,618 filed Jun. 23, 1993, now U.S. Pat. No. 5,472,712, and of U.S. patent application Ser. No. 08/086,248 filed Jul. 1, 1993, abandoned, both of which are continuations-in-part of U.S. patent application Ser. No. 07/814,111, filed Dec. 24, 1991, now U.S. Pat. No. 5,273,760. U.S. application Ser. No. 08/133,503 is also a continuation-in-part of U.S. patent application Ser. No. 08/097,558 filed Jul. 27, 1993, now U.S. Pat. No. 5,580,578, which in turn is a continuation-in-part of U.S. Ser. No. 07/826,084 filed Jan. 27, 1992, now U.S. Pat. No. 5,286,493.

Thus, the '551 patent was first filed in its entirety on October 7, 1993, as it is a

continuation-in-part of the applications with the earlier filing date. As October 7, 1993 is after the filing date of the present invention, any new material added to the application as of October 7, 1993 is not available to be cited as 102(e) art. Any information contained in the '551 patent available to be cited under 102(e) must be entitled to priority to the parent applications related by continuation-in-part, prior to July 1, 1993. Therefore, the specifications of U.S. Patent Nos. 5,273,760; 5,286,493; and 5,472,712; of which U.S. Patent No. 5,698,551 claims priority by continuation-in-part, will be considered with respect to this rejection.

Assuming arguendo that U.S. Patent Nos. 5,273,760; 5,286,493; and 5,472,712 are prior art under 35 U.S.C. § 102(e), it is respectfully submitted that these patents fail, at the very least, to recite or suggest all of the following limitations of independent claim 6 of the present application:

> *(i)...wherein the dissolution rate in-vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37° is from about 12.5% to about 42.5% (by wt) opioid released after 1 hour, from about 25% to about 65% (by wt) opioid released after 2 hours, from about 45% to about 85% (by wt) opioid released after 4 hours and greater than 60% (by wt) opioid released after 8 hours, the in-vitro release rate being substantially independent of pH in that a difference, at any given time, between an amount of opioid released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,...*
>
> *(ii)...the in-vitro release rate being chosen such that the peak plasma level of said opioid obtained in-vivo occurs at least 4 to about 8 hours after administration of the dosage form,...*
>
> *(iii)...said dosage form and providing an extended duration of therapeutic effect of about 24 hours.*

Therefore, it is respectfully submitted that the claims of the present invention would not be anticipated or obvious in view of U.S. Patent Nos. 5,273,760; 5,286,493; 5,472,712 and the

102(e) rejection over U.S. Patent No. 5,698,551 should be removed.

U.S. Patent No. 5,133,974 (Paradissis et al.)

Claims 6-15, 18-19 were rejected under 35 U.S.C. § 102(e) on the grounds of being anticipated by U.S. Patent No. 5,133,974 (Paradissis et al.).

This rejection is respectfully traversed. It is respectfully submitted that the Paradissis et al. patent describes certain extended release pharmaceutical formulations which are adapted to approach zero order release of drug over a 12 to at least 24 hour period. The formulation comprises a mixture of immediate release particles containing a drug, inert substrate and binder, coated with talc, and extended release particles which are the same as the immediate release particles with a dissolution modifying coating, e.g., ethylcellulose. At column 4, lines 26-59, it is stated that the formulations described therein may be used for a "wide variety of medicaments..." including narcotics such as morphine, etc. However, no opioid analgesic formulations are exemplified, and it is respectfully submitted that there is no hint or suggestion in this reference of the presently claimed method of treatment having the specified pharmacokinetic parameters.

U.S. Patent No. 5,266,331 (Oshlack et al.)

Claims 6-19 and 21-23 were rejected under 35 U.S.C. § 102(e) on the grounds of being anticipated by U.S. Patent No. 5,266,331 (Oshlack et al).

This rejection is respectfully traversed. U.S. Patent No. 5,266,331 to Oshlack et al. relates to controlled release oxycodone compositions for which a peak plasma level of oxycodone is obtained *in vivo* between 2 and 4 hours after administration. The '331 patent notes that the formulations described therein provide "at least 12 hours pain relief". Moreover, the steady state clinical data described in the '311 patent (see Example 13) indicates that the exemplified oxycodone formulations were dosed every 12 hours. In contrast, the claimed

invention provides a peak plasma level of the opioid in vivo at least 4 to about 8 hours after administration of the dosage form, and provides a duration of effect of about 24 hours.

Accordingly, this reference does not teach or suggest to one of ordinary skill in the art to provide a peak plasma level of at least 4 to about 8 hours after administration of the dosage form to provide a duration of effect of about 24 hours based on U.S. Patent No 5,266,331, which discusses the peak plasma level of between 2 and 4 hours after administration for at least 12 hours pain relief, and which exemplifies only 12 hour oxycodone formulations. Thus, there is no teaching or suggestion in U.S. Patent No. 5,266,331 to lead one skilled in the art to arrive at the presently claimed invention.

U.S. Patent No. 5,681,585 (Oshlack et al.)

Claims 6-13, 18-19 were rejected under 35 U.S.C. § 102(e) on the grounds of being anticipated by U.S. Patent No. "5,685,585" (*sic*, 5,681,585) to Oshlack et al.

This rejection is respectfully traversed. U.S. Patent No. 5,681,585 was filed on June 20, 1996 and is a continuation-in-part of U.S. application Ser. No. 08/561,829 filed Nov. 27, 1995, which is a continuation of U.S. application Ser. No. 08/086,248 filed on Jul. 1, 1993, abandoned, which is a continuation-in-part of U.S. application Ser. No. 07/814,111, filed Dec. 24, 1991, now U.S. Pat. No. 5,273,760.

Thus, the '585 patent was first filed in its entirety on June 20, 1996, as it is a continuation-in-part of the applications with the earlier filing dates. As June 20, 1996 is after the filing date of the present application, any new material added to the application as of June 20, 1996 is not available to be cited as 102(e) art. Any information contained in the '585 patent available to be cited under 102(e) must be entitled to priority to the parent applications related by continuation-in-part, prior to July 1, 1993. Therefore, the specification of U.S. Patent No. 5,273,760, of which the '585 patent claims priority by continuation-in-part, will be considered

with respect to this rejection.

For the reasons stated above with respect to the rejection over the'551 patent, assuming arguendo that U.S. Patent No. 5,273,760 is prior art under 35 U.S.C. § 102(e), it is respectfully submitted that the claims of the present invention would not be anticipated or obvious in view of U.S. Patent Nos. 5,273,760 and the 102(e) rejection over U.S. Patent No. 5,681,585 should be removed.

U.S. Patent No. 4,844,909 (Goldie et al.)

Claims 6-8, 11-19, and 21-23 were rejected under 35 U.S.C. § 102(b) on the grounds of being anticipated by U.S. Patent No. 4,844,909 (Goldie et al).

This rejection is respectfully traversed. U.S. Patent No. 4,844,909 to Goldie et al. relates to controlled release hydromorphone formulations (e.g., controlled-release matrix compositions and spheroid compositions) for which a peak plasma level of hydromorphone is obtained *in vivo* between 2 and 4 hours after administration and provides "therapeutic levels of hydromorphone in vivo over at least a 12 hour period, and may therefore be used on a twice daily basis."

The present invention as recited in claims 6-23 are directed to methods of treating pain with formulations which provide a peak plasma level of the opioid in vivo of at least 4 to about 8 hours after administration of the controlled-release matrix dosage form which is not taught or suggested by Goldie. The present claims also recite that the formulations provide an extended duration of effect of about 24 hours, which is not taught or suggested from the 12 hour formulations disclosed in Goldie.

In view of the above, it is respectfully requested that all of the Examiner's 35 U.S.C. §102 rejections be withdrawn.

III. Rejections under 35 U.S.C. §103(a)

Claims 6-23 were rejected under 35 U.S.C. § 103(a) on the grounds of being unpatentable over U.S. Patent No. 4,844,909 to Goldie et al. in view of U.S. Patent No. 5,958,551 to Oshlack et al. or U.S. Patent No. 5,266,331 to Oshlack et al.

These rejections are respectfully traversed. In accordance with 35 U.S.C. § 103(c), U.S. Patent Nos. 5,958,551 and 5,266,331 are not available as prior art against the present application as the prior art and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

In view of the above, it is respectfully requested that the Examiner's 35 U.S.C. §103(a) rejections be withdrawn.

IV. Conclusion

It is now believed that the above-referenced rejections have been obviated and it is respectfully requested that the rejections be withdrawn. It is believed that all pending claims are now in a condition for allowance.

The Examiner is invited to contact the undersigned at the telephone number provided below if it is determined that any further issues remain.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,

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